

--The TTSEs form surprisingly stable trimeric molecules (Examples 2, 3, and 4). The experimental observations, that (1) a substantial part of the recombinant proteins exists in the oligomeric state of, and can be cross-linked as, trimeric molecules even at 70°C and (2) that exchange of monomers between different trimers can only be detected after exposure to elevated temperature are evidence of a extremely high stability of the tetranectin trimerising structural element. This feature must be reflected in the amino acid sequence of the structural element. In particular, the presence and position of the glutamine containing repeat in the sequential array of heptad repeats is, together with the presence and relative position of the other conserved residues in the consensus sequence (Fig. 2), considered important for the formation of these stable trimeric molecules. For most practical uses the cysteine residue 50 should be mutagenized to serine, threonine, methionine or to any other amino acid residue in order to avoid formation of an unwanted inter-chain disulphide bridge, which eventually would lead to uncontrolled multimerisation, aggregation and precipitation of a polypeptide product harbouring this sequence.--

At Page 57, after line 10, please incorporate the following Abstract in its entirety. The abstract finds support throughout the specification as originally filed. The abstract was further included in the related application PCT/DK98/00245, from which the present application is derived as national stage under 35 U.S.C. § 371.

--ABSTRACT

The present invention relates to the design of trimeric polypeptides using polypeptide structural elements derived from the tetranectin protein family, and their use in rational de novo design and production of multi-functional molecules including the application of the multi-functional molecules in protein library technology, such as phage display technology, diagnostic and therapeutic systems, such as human gene therapy and imaging. The trimeric polypeptides being constructed as a monomer polypeptide construct comprising at least one tetranectin trimerising structural element (TTSE) which is covalently linked to at least one heterologous moiety, said TTSE being capable of forming a stable complex with two other TTSEs; or as an oligomer which is comprised of two monomer polypeptide constructs as mentioned above, and which comprises three TTSEs or a multiplum of three TTSEs, or which is comprised of three monomer polypeptide constructs.--